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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/643,752	08/19/2003	David R. Liu	LS5-001	4082
51414	7590	06/27/2006		
GOODWIN PROCTER LLP PATENT ADMINISTRATOR EXCHANGE PLACE BOSTON, MA 02109-2881				EXAMINER MUMMERT, STEPHANIE KANE
				ART UNIT 1637 PAPER NUMBER

DATE MAILED: 06/27/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/643,752	LIU ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Stephanie K. Mummert, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 6/10/05.
- 2a) This action is **FINAL**.                    2b) This action is non-final.
- 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 24-48 and 104 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) Claim(s) \_\_\_\_\_ is/are allowed.
- 6) Claim(s) 24-48 and 104 is/are rejected.
- 7) Claim(s) \_\_\_\_\_ is/are objected to.
- 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.
- 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  - a) All    b) Some \* c) None of:
    1. Certified copies of the priority documents have been received.
    2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
    3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>5/9/05; 6/10/05</u> . | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|  | 6) <input type="checkbox"/> Other: _____                                    |

## **DETAILED ACTION**

The preliminary amendment filed January 20, 2004 canceling claims 1-23 and 49-103 and adding claim 104 is acknowledged and has been entered. Claims 24-48 and 104 are pending and will be examined.

Please note that the Examiner of record has changed. Please address all future correspondence to Examiner Stephanie Mummert, whose contact information is included at the conclusion of this action.

### ***Information Disclosure Statement***

1. The information disclosure statements (IDS) submitted on May 9, 2005 and June 10, 2005 are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner.

### ***Double Patenting***

2. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 24, 30-31, 36-37, 41 and 104 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-51, 82-83, 85-87 and 95 of copending Application No. 10/101030 in view of Sergeev. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application and the copending application are drawn to a method wherein a template directs the synthesis of a reaction product, through the binding of transfer units to anti-codon sequences within the template and with reactive units attached to the transfer units.

The claims differ from one another in that the claims of the instant application are directed to a method of increasing reaction selectivity among multiple reactants and it is not explicitly stated within the claim that the method is carried out *in vitro*. However, the method steps of the instant application accomplish nucleic acid templated synthesis, in addition to increasing reaction selectivity. Furthermore, the specification of the instant application discloses that the method may be performed *in vitro*.

Finally, while claim 47 of the copending application is directed specifically to a reaction between first and second reactive units, and claims 24, 37 and 104 recite up to three or four reactive units, considering claim 95, a plurality of reactive units and a plurality of templates may be incorporated into the method of producing different reaction products. Therefore, it would be obvious to incorporate more than the first two reactive units into the method described in the instant application and the copending application. Furthermore, considering the teaching of

Sergeev, wherein a plurality of transfer units with a plurality of reactive units are contemplated for template directed synthesis reactions (p. 15 top diagram where up to 'n' oligomer transfer units are disclosed). Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to extend the broad teachings of claim 95 of the copending application, in light of the teachings of Sergeev to arrive at the claims of the instant application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

4. Claims 24-28 and 104 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47-48 and 54 of copending Application No. 10/949162. Although the conflicting claims are not identical, they are not patentably distinct from each other. The claims of the copending application represent a broader scope of the claims of the instant application.

In the copending application, the claims are directed to a method for the synthesis of a library of chemical compounds comprising steps wherein a plurality of templates, a plurality of reactive units and a plurality of transfer units are incorporated in the method. In the instant application, a specific combination of transfer units and reactive units are claimed which are used in a method of template directed synthesis wherein the reaction selectivity is enhanced. The inclusion of multiple reactive units and transfer units within the claims of the instant application would fall within the scope of the plurality of components claimed in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

5. Claims 24-28 and 104 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 47 and 64 of copending Application No. 10/949163. Although the conflicting claims are not identical, they are not patentably distinct. The claims of the copending application differ from the claims of the instant application in that the claims of the copending application are amended to explicitly claim that the method of synthesis is directed to the formation of a small molecule and the claims incorporate small molecule scaffolds in place of the term ‘reactive unit’ in the instant application. However, while the term ‘reactive unit’ is not given an explicit definition, the term is taught as “a reactive unit (e.g., a scaffold molecule)” (paragraph 11 of PgPub of instant application), therefore, it would be obvious that a small molecule comprising small molecule scaffolds and building blocks would result from the practice of the method claimed in the instant application and in the copending application.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

#### *Claim Interpretation*

The term ‘reactive unit’ is being given the broadest reasonable interpretation in light of the specification. As the term is not explicitly defined and is instead referred to in terms such as “a reactive unit (e.g., a scaffold molecule)” (paragraph 11 of PgPub). While this term “scaffold molecule” is defined as “a chemical compound having at least one site or chemical moiety suitable for functionalization. The small molecule scaffold or molecular scaffold may have two,

three, four, five or more sites or chemical moieties suitable for functionalization. These functionalization sites may be protected or masked as would be appreciated by one of skill in this art. The sites may also be found on an underlying ring structure or backbone.” (paragraph 42 of PgPub).

Also, it is not clear from the specification that the term does not encompass nucleotides or nucleic acid molecules, the term is being interpreted broadly as encompassing nucleic acid templated synthesis techniques which include ligation reactions between nucleotides.

***Claim Rejections - 35 USC § 102***

6. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

7. Claims 24, 30-37, 41-48 and 104 are rejected under 35 U.S.C. 102(b) as being anticipated by Sergeev (WO00/61775; October 2000). Sergeev teaches a method of syntheses of biologically active substances based on the hybridization of two or more oligomers which are bound with biologically active precursors which interact to form a biologically active substance (Abstract).

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With regard to claim 24, Sergeev teaches a method of increasing reaction selectivity among a plurality of reactants in a nucleic acid-templated synthesis, the method comprising the steps of:

- (a) providing (i) a template comprising a first reactive unit associated with a first oligonucleotide comprising a predetermined codon sequence, (ii) a first transfer unit comprising a second reactive unit associated with a second oligonucleotide comprising an anti-codon sequence capable of annealing to said codon sequence, and (iii) a second transfer unit comprising a third reactive unit different from said second reactive unit associated with a third oligonucleotide without an anti-codon sequence capable of annealing to said codon sequence (p. 11-17, where the binding of multiple transfer units capable of binding to a template with separate codon sequences are present are linked to multiple reactive units; see also Figures 1-10 and p. 21-24, where the Figures are described); and
- (b) mixing said template, said first transfer unit and said second transfer unit under conditions to permit annealing of said second oligonucleotide of said first transfer unit to said first oligonucleotide of said template thereby to enhance covalent bond formation between said second reactive unit and said first reactive unit relative to covalent bond formation between said third reactive unit and said first reactive unit (p. 11-17, where the binding of multiple transfer units capable of binding to a template with separate codon sequences are present are linked to multiple reactive units; see third step where a chemical bond forms between reactive units).

With regard to claim 37, Sergeev teaches a method of increasing reaction selectivity among a plurality of reactants in a nucleic acid-templated synthesis, the method comprising the steps of:

(a) providing (i) a template comprising a first oligonucleotide comprising first and second codon sequences, (ii) a first transfer unit comprising a first reactive unit associated with a second oligonucleotide comprising a first anti-codon sequence capable of annealing to said first codon sequence, (iii) a second transfer unit comprising a second reactive unit associated with a third oligonucleotide comprising a second anti-codon sequence capable of annealing to said second codon sequence, and (iv) a third transfer unit comprising a third reactive unit associated with a fourth oligonucleotide sequence without an anti-codon sequence capable of annealing to said first codon sequence or said second codon sequence (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units); and

(b) mixing said template, said first transfer unit, said second transfer unit and said third transfer unit under conditions to permit annealing of said first anti-codon sequence to said first codon sequence and said second anti-codon sequence to said second codon sequence thereby to enhance covalent bond formation between said first reactive unit and said second reactive unit relative to covalent bond formation between said third reactive unit and said first reactive unit or between said third reactive unit and said second reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units; see step where chemical bond is formed between reactive units).

With regard to claim 30, Sergeev teaches an embodiment of claim 24, wherein said first reactive unit is covalently attached to said first oligonucleotide (p. 11-17, where the binding of multiple transfer units capable of binding to a template with separate codon sequences are present are linked to multiple reactive units; see p. 11-17, where the linking moieties are

described and wherein these moieties covalently link the reactive unit to their respective oligomer).

With regard to claim 31 and 41, Sergeev teaches an embodiment of claim 24 and 37, wherein said second reactive unit is covalently attached to said second oligonucleotide (p. 11-17, where the binding of multiple transfer units capable of binding to a template with separate codon sequences are present are linked to multiple reactive units; see p. 11-17, where the linking moieties are described and wherein these moieties covalently link the reactive unit to their respective oligomer).

With regard to claim 32 and 42, Sergeev teaches an embodiment of claim 24 and 37, wherein said third reactive unit is covalently attached to said third oligonucleotide (p. 11-17, where the binding of multiple transfer units capable of binding to a template with separate codon sequences are present are linked to multiple reactive units; see p. 11-17, where the linking moieties are described and wherein these moieties covalently link the reactive unit to their respective oligomer).

With regard to claim 33, Sergeev teaches an embodiment of claim 24, wherein said second reactive unit and said third reactive unit are capable of reacting independently with said first reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units, where first and second reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 34, Sergeev teaches an embodiment of claim 24, wherein said second reactive unit and said third reactive unit are capable of reacting with one another (see p. 15, for example, where the second and third reactive units react with one another).

With regard to claim 35, Sergeev teaches an embodiment of claim 34, wherein the reaction between said second reactive unit and said third reactive unit are incompatible with their respective reactions with said first reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units, where first and second reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 36, Sergeev teaches an embodiment of claim 24, comprising providing a plurality of transfer units (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units and where 'n' is a plurality of transfer units).

With regard to claim 43, Sergeev teaches an embodiment of claim 37, wherein said third reactive unit is covalently attached to said fourth oligonucleotide (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units and where the linking moieties are described and wherein these moieties covalently link the reactive unit to their respective oligomer).

With regard to claim 44, Sergeev teaches an embodiment of claim 37, wherein said third reactive unit is capable of reacting with said first reactive unit or said second reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to

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respective reactive units, where second and third reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 45, Sergeev teaches an embodiment of claim 37, wherein said third reactive unit is capable of reacting with said first reactive unit and said second reactive unit (p. 15-17 and Figure 4 and 8-10, where up to ‘n’ transfer units are described which are attached to respective reactive units, where second and third reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 46, Sergeev teaches an embodiment of claim 44 or 45, wherein the reaction between said third reactive unit and said first reactive unit is incompatible with the reaction between said first reactive unit and said second reactive unit (p. 15-17 and Figure 4 and 8-10, where up to ‘n’ transfer units are described which are attached to respective reactive units, where second and third reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 47, Sergeev teaches an embodiment of claim 44 or 45, wherein the reaction between said third reactive unit and said second reactive unit is incompatible with the reaction between said first reactive unit and said second reactive unit (p. 15-17 and Figure 4 and 8-10, where up to ‘n’ transfer units are described which are attached to respective reactive units, where second and third reactive units are capable of reacting, p. 15, and wherein first and third reactive units are capable of reacting – see Figure 4).

With regard to claim 48, Sergeev teaches an embodiment of claim 37, wherein said covalent bond formation between said first reactive unit and said second reactive unit is via a regioselective distance dependent reaction (p. 15, for example, where it is noted that the distance

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between oligomers is between 0 to 7 nucleotides; Figure 1, where the reaction is selective in that the reactive units have to be in the proper selective position for reaction to occur).

With regard to claim 104, Sergeev teaches an embodiment of claim 24, further comprising:

providing a second template comprising a fourth reactive unit associated with a fourth oligonucleotide comprising a second predetermined codon sequence, different from said predetermined codon sequence of said first oligonucleotide, wherein said second predetermined codon sequence is capable of annealing with said third oligonucleotide; and mixing said second template with said first transfer unit, said second transfer unit, and said template comprising said first reactive unit associated with said first oligonucleotide under conditions to permit annealing of said second oligonucleotide of said first transfer unit to said first oligonucleotide of said template and, in the same solution, annealing of said third oligonucleotide of said second transfer unit to said fourth oligonucleotide of said second template, thereby to induce covalent bond formation both between said second reactive unit and said first reactive unit and between said fourth reactive unit and said third reactive unit (p. 15-17 and Figure 4 and 8-10, where up to 'n' transfer units are described which are attached to respective reactive units; see step where chemical bond is formed between reactive units, including a reaction between first and second reactive units and between third and fourth reactive units).

8. Claims 24-40 are rejected under 35 U.S.C. 102(b) as being anticipated by Koster et al. (US Patent 6,043,031; March 2000). Koster teaches a method of forming a linkage between

adjacent oligonucleotides bound to a template through the action of a ligase enzyme (Abstract; Figure 5).

With regard to claim 24, Koster teaches a method of increasing reaction selectivity among a plurality of reactants in a nucleic acid-templated synthesis, the method comprising the steps of:

(a) providing (i) a template comprising a first reactive unit associated with a first oligonucleotide comprising a predetermined codon sequence, (ii) a first transfer unit comprising a second reactive unit associated with a second oligonucleotide comprising an anti-codon sequence capable of annealing to said codon sequence, and (iii) a second transfer unit comprising a third reactive unit different from said second reactive unit associated with a third oligonucleotide without an anti-codon sequence capable of annealing to said codon sequence (Figure 5, where two transfer units with free ‘reactive units’ at their respective 5’ and 3’ ends are bound to a template); and

(b) mixing said template, said first transfer unit and said second transfer unit under conditions to permit annealing of said second oligonucleotide of said first transfer unit to said first oligonucleotide of said template thereby to enhance covalent bond formation between said second reactive unit and said first reactive unit relative to covalent bond formation between said third reactive unit and said first reactive unit (Figure 5, where a bond between the reactive units of the first and second transfer unit is formed by ‘LCR’).

With regard to claims 25, Koster teaches an embodiment of claim 24, wherein said template is associated with a capturable moiety (Figure 5, where the ‘template’ incorporates a template capture sequence, TCS1 or 2).

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With regard to claim 26, Koster teaches an embodiment of claim 24, wherein said first transfer unit is associated with a capturable moiety (Example 6, col. 24, where oligo C is biotinylated, and where the designation first and second transfer unit is arbitrary).

With regard to claim 27, Koster teaches an embodiment of claim 24, wherein said second transfer unit is associated with a capturable moiety (Example 6, col. 24, where oligo C is biotinylated, and where the designation first and second transfer unit is arbitrary).

With regard to claim 28, Koster teaches an embodiment of claim 25, 26 or 27 wherein said capturable moiety is selected from the group consisting of biotin, avidin and streptavidin (Example 6, col. 24, where oligo C is biotinylated, and where the designation first and second transfer unit is arbitrary).

With regard to claim 29, Koster teaches an embodiment of claim 28, further comprising the step of capturing said capturable moiety (Figure 5, where the products are captured to the array).

With regard to claim 30, Koster teaches an embodiment of claim 24, wherein said first reactive unit is covalently attached to said first oligonucleotide (Figure 5, where two transfer units with free ‘reactive units’ at their respective 5’ and 3’ ends are bound to a template and where the reactive ends would inherently be covalently attached to the oligonucleotide).

With regard to claim 31, Koster teaches an embodiment of claim 24, wherein said second reactive unit is covalently attached to said second oligonucleotide (Figure 5, where two transfer units with free ‘reactive units’ at their respective 5’ and 3’ ends are bound to a template and where the reactive ends would inherently be covalently attached to the oligonucleotide).

With regard to claim 32, Koster teaches an embodiment of claim 24, wherein said third reactive unit is covalently attached to said third oligonucleotide (Figure 5, where two transfer units with free ‘reactive units’ at their respective 5’ and 3’ ends are bound to a template and where the reactive ends would inherently be covalently attached to the oligonucleotide).

With regard to claim 33, Koster teaches an embodiment of claim 24, wherein said second reactive unit and said third reactive unit are capable of reacting independently with said first reactive unit (Figure 5, where two transfer units with free ‘reactive units’ at their respective 5’ and 3’ ends are bound to a template and are capable of reacting with one another reactive unit).

With regard to claim 34, Koster teaches an embodiment of claim 24, wherein said second reactive unit and said third reactive unit are capable of reacting with one another (Figure 5, where two transfer units with free ‘reactive units’ at their respective 5’ and 3’ ends are bound to a template and are capable of reacting with one another reactive unit).

With regard to claim 35, Koster teaches an embodiment of claim 34, wherein the reaction between said second reactive unit and said third reactive unit are incompatible with their respective reactions with said first reactive unit (Figure 5, where two transfer units with free ‘reactive units’ at their respective 5’ and 3’ ends are bound to a template and where ligation only occurs between two reactive units at a time on a template in the method disclosed by Koster).

With regard to claim 36, Koster teaches an embodiment of claim 24, comprising providing a plurality of transfer units (Figure 5, bottom panel where a multitude of captured ‘reacted’ products are captured on an ‘ordered array; see also col. 6, line 66 to col. 7 line 3, where the multiplex format is described).

With regard to claim 40, Koster teaches an embodiment of claim 38, wherein said capturable moiety is a reaction product resulting from a reaction between said first reactive unit and said second reactive unit when said first transfer unit and said second transfer unit are annealed to said template (Figure 5, where the reacted/ligated product is capturable after the reaction occurs).

***Claim Rejections - 35 USC § 103***

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

10. Claims 25-29 and 38-40 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sergeev (WO00/61775; October 2000) as applied to claims 24, 37 and 104 above, and further in view of Koster et al. (US Patent 6,043,031; March 2000). Sergeev teaches a method of syntheses of biologically active substances based on the hybridization of two or more oligomers which are bound with biologically active precursors which interact to form a biologically active substance (Abstract).

Sergeev teaches the limitations of claims 24, 30-37, 41-48 and 104 as recited in the 102 rejection stated above. However, Sergeev does not teach explicitly that the template or the transfer units are associated with capturable moieties. Koster teaches a method of forming a

linkage between adjacent oligonucleotides bound to a template through the action of a ligase enzyme (Abstract; Figure 5).

With regard to claims 25 and 38, Koster teaches an embodiment of claim 24 and 37, wherein said template is associated with a capturable moiety (Figure 5, where the ‘template’ incorporates a template capture sequence, TCS1 or 2).

With regard to claim 26, Koster teaches an embodiment of claim 24, wherein said first transfer unit is associated with a capturable moiety (Example 6, col. 24, where oligo C is biotinylated, and where the designation first and second transfer unit is arbitrary).

With regard to claim 27, Koster teaches an embodiment of claim 24, wherein said second transfer unit is associated with a capturable moiety (Example 6, col. 24, where oligo C is biotinylated, and where the designation first and second transfer unit is arbitrary).

With regard to claim 28 and 39, Koster teaches an embodiment of claim 25, 26, 27 or 38 wherein said capturable moiety is selected from the group consisting of biotin, avidin and streptavidin (Example 6, col. 24, where oligo C is biotinylated, and where the designation first and second transfer unit is arbitrary).

With regard to claim 29, Koster teaches an embodiment of claim 28, further comprising the step of capturing said capturable moiety (Figure 5, where the products are captured to the array).

With regard to claim 40, Koster teaches an embodiment of claim 38, wherein said capturable moiety is a reaction product resulting from a reaction between said first reactive unit and said second reactive unit when said first transfer unit and said second transfer unit are

annealed to said template (Figure 5, where the reacted/ligated product is capturable after the reaction occurs).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have modified the technique of template-directed synthesis of molecules, including RNA, proteins and small molecules as taught by Sergeev to incorporate the inclusion of capturable moieties as taught by Koster to arrive at the claimed invention with a reasonable expectation for success. As taught by Sergeev, “Only 14 peptides chemically bound to 14 oligomers are required to synthesize p53 tumour suppressor specifically in the cells of the ovarian tumour. In any type of tumour RNAs specific to this cell type are expressed. By this method it is possible to synthesize any protein or BACs described above on these RNAs” (p. 32, lines 27-32). While the method disclosed by Sergeev is designed specifically to target peptides or BACs to specific cell types, incorporating a capturable moiety to one or more transfer units such as biotin as described by Koster would allow for the isolation of the p53 peptide synthesized from the specific cells in which the synthesis is designed to occur, prior to the degradation of the oligomers associated with the transfer units (p. 33, lines 7-9). Therefore, it would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have included the capturable moieties disclosed by Koster in order to achieve isolation of the products of the synthesis reaction with a reasonable expectation for success.

### ***Conclusion***

No claims are allowed.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. include Landegren et al. (Science, 1988, vol. 241, no. 4869, p. 1077-1080) teaches an assay for the detection of a specific DNA sequence based on the ability of oligonucleotides to anneal adjacent to one another on a target DNA molecule (Abstract). Gartner and Liu (J. Am. Chem. Soc., 2001, vol. 123, p. 6961-6963) describe a method in which DNA supports DNA templated synthesis of reaction products (Figure 1). Bruick et al. (Current Biology, 1996, vol. 3, p. 49-56) describe a method for chemical ligation of peptides to oligonucleotides in a template directed reaction (Abstract). Summerer and Marx (Angew. Chem. Int. Ed. 2002, vol. 41, no. 1, p. 89-90) review the field of DNA templated synthesis (Schemes 1-4 and Figure 1).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephanie K. Mummert, Ph.D. whose telephone number is 571-272-8503. The examiner can normally be reached on M-F, 8:30-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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